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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,606	02/21/2006	Hans G. Boman	3612.1001-000	9912

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EXAMINER	
SWARTZ, RODNEY P	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,606	BOMAN ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *9-11,3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12,14-20,22,23,25-27,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,3-8,12,19,20,22,23 and 25-27* is/are allowed.

6)☒ Claim(s) *9-11,14-18,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 March 2008 has been entered.

2. Claims 1, 10, and 31 have been amended.

3. Claims 1, 3-12, 14-20, 22, 23, 25-27, 31, and 32 are pending and under consideration.

Rejections Withdrawn

4. The rejection of claims 1, 3-8, 10-12, and 20, 22, 23, and 25-27 under 35 U.S.C. 112, second paragraph, as being indefinite for "levels" is withdrawn in light of the amendment of the claims.

Rejections Maintained

5. The rejection of claims 9, 14-19, and 31 under 35 U.S.C. 112, first paragraph, scope of enablement for compositions for or methods of treatment *in vivo*, is maintained.

Applicants argue that at the priority date, LL-37 had been demonstrated in the art to be successfully delivered *in vivo* either by injection of the peptide or by delivery of a nucleic acid encoding LL-37 such that the LL-37 retained biological activities. Applicants cite Koczulla et al, Bals et al, and Mosca et al, as supportive documentation.

The examiner has considered applicants' arguments in light of the cited references, but does not find them persuasive.

The instant claims 9 and 14-18 are drawn to "A method of treating an individual to reduce the risk of infection".

None of the cited references teach a method of pretreatment of an individual to "reduce the risk of infection". Koczulla et al only teach angiogenic roles for injected LL-37 while referring to the antimicrobial activity of LL-37. Bals et al teach that fluids obtained from xenografts in mice have increased LL-37 *in vitro* antimicrobial activity when the xenografts are exposed to adenovirus expressing LL-37. Mosca et al do not teach LL-37 at all.

Thus, neither the cited references nor the instant specification teach methods of reducing the risk of infection in susceptible individuals by administration of LL-37.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 10, 11, and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for the determination of levels of LL-37 in body fluids and *in vitro* methods for bactericidal assays utilizing LL-37, does not reasonably provide enablement for compositions for or methods of treatment *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of

experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention - Claims 10 and 11 are drawn to a two step method. Step 1 is determining a level of LL-37 in a subject. Step 2 is pretreatment of said subject to reduce the risk of infection comprising administration of an amount of LL-37. Claim 32 is drawn to a method of treating an infection in a subject by administration of a therapeutically effective amount of LL-37.

The state of the prior art - teaches that LL-37 is an antimicrobial peptide found in human neutrophils and expressed in skin and gingiva and appears to play an important role in defense against invading pathogens (Weinberg et al, Crit. Rev. Oral Biol. Med., 9(4):399-414, 1998). However, at the time of filing of the instant application, the art did not provide clinical or experimental *in vivo* information concerning treatment of infection or prophylactic administration of LL-37 to subjects. Thus, there is a lack of predictability in the art for treatments of subjects by administration of LL-37.

The specification teaches methods for the determination of levels of LL-37 in body fluids and *in vitro* methods for bactericidal assays utilizing LL-37. However, the specification is insufficient for the extremely broad scope of the instant claims, i.e., *in vivo* treatment of current infections or prophylactic treatment of subjects with administration of LL-37. For instance, the specification provides no dose regimen, composition parameters, effective dose levels needed for *in vivo* efficacy, or tissue availability.

Thus, the extremely broad treatment scope of the instant claims constitute merely an invitation to experiment without a reasonable expectation of success.

Conclusion

7. Claims 9-11, 14-18, and 31-32 are rejected.

8. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Wednesday from 9:00 AM to 7:30 PM EST. Thursday is the examiner's work at home day.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Shannon Foley, can be reached on (571)272-0898.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rodney P. Swartz, Ph.D./

Primary Examiner, Art Unit 1645

June 10, 2008